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Mortality trends in men and women with acute myocardial infarction in coronary care units in Israel

A comparison between 1981–1983 and 1992–1994

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Aims To assess trends in the management and subsequent outcome in men and women in two cohorts of consecutive patients with acute myocardial infarction hospitalized in coronary care units in Israel, in the pre-reperfusion and the reperfusion eras.

Methods and Results We compared trends in the in-hospital management, and 30-day and 1-year mortality in men and women in two cohorts of patients hospitalized with acute myocardial infarction in coronary care units in Israel, in the pre-reperfusion and the reperfusion eras. The first cohort of 5839 consecutive patients (4315 men, 74%) was from the Secondary Prevention Reinfarction Israeli Nifedipine Trial (SPRINT) registry of 1981–1983; the second cohort of 1940 patients (1429 males, 74%) derived from two prospective nationwide surveys conducted in all coronary care units in Israel in January/February 1992 and 1994. The demographic and clinical characteristics of patients with acute myocardial infarction in both periods were comparable. Patients in 1992–94 received aspirin, angiotensin-converting enzyme inhibitors, beta-blockers and nitrates more frequently than in 1981–83. Thrombolysis, coronary angiography, angioplasty and bypass grafting were not used in 1981–83, whereas in 1992–94 these procedures were used in 45%, 28%, 11% and 4% of men, respectively, and in 39%, 20%, 9% and 3% of women, respectively. The 30-day age-adjusted mortality declined, in men, from 17·0% in 1981–83 to 10·8% in 1992–94 (multivariate-adjusted odds ratio [OR]=0·69; 95% confidence interval [CI] 0·55 to 0·87), and the cumulative 1-year age-adjusted mortality declined from 24·6% to 16·9% (adjusted hazard ratio [HR]=0·70%; 95% CI 0·60 to 0·81). In women, the decline in mortality rates were of similar magnitude, from 24·0% to 15·1% (OR=0·70; 95% CI 0·52 to 0·94), and from 33·6% to 21·0% (HR=0·67; 95% CI 0·55 to 0·81), respectively. In both sexes, the decline in mortality was more marked in patients reperfused by thrombolysis and/or mechanical revascularization, but was also evident in non-reperfused patients.

Conclusions Despite higher mortality in both periods in women compared to men, the prognosis of men and women with acute myocardial infarction improved considerably during the last decade, with a similar decline in 1-year mortality of $\approx$30%. The implementation in daily practice of new therapeutic modalities proven to be effective in clinical trials after acute myocardial infarction, probably played a major role in this favourable outcome in both sexes.
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Key Words: Sex, survival, myocardial infarction, reperfusion, thrombolysis.

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Introduction

New important therapies for the management of patients with an acute myocardial infarction were introduced during the last decade. The beneficial effects of early reperfusion with thrombolytic therapy or coronary angioplasty (PTCA) on short- and long-term mortality rates are now well established[1–4]. The reperfusion era also embraces the extensive use of aspirin, beta-blocker agents, vasodilator therapy, and the common use of ACE-inhibitors, medications convincingly shown to reduce morbidity and mortality after acute myocardial infarction[2,4–6].

In recent years, several studies reported a decline in early mortality after acute myocardial infarction[7–22]. However, studies comparing the early- and post-discharge outcome of patients with acute myocardial infarction before and after the advent of the reperfusion era are scarce[15,17,22]. It is also unclear whether the decline in mortality was of similar magnitude in men and women. This latter issue is of interest, since several previous studies demonstrated that even after controlling for baseline differences, women fare worse than men[22–28].

The purpose of the present study was to determine trends in the management, in-hospital complications, and 30-day and first-year mortality, separately in men and women in two cohorts of patients hospitalized for acute myocardial infarction in the coronary care units in Israel, one during 1981–83 (pre-reperfusion era) and the other during 1992–94 (reperfusion era).

Methods

Patients

Two cohorts of unselected patients hospitalized in the coronary care units in Israel with a confirmed diagnosis of acute myocardial infarction constitute the basis for this study. The first cohort encompasses 5839 (4315 men, 74%) consecutive acute myocardial infarction patients with a confirmed acute myocardial infarction who were hospitalized in 13 of the 21 coronary care units operating in Israel between 1981 and 1983 and constitute the Secondary Prevention Reinfarction Israeli Nifedipine Trial [SPRINT] Registry[23]. Two-thousand and seventy-six patients were included in SPRINT. The detailed methods and results of SPRINT have been published elsewhere[29]. In brief, SPRINT examined the use of prophylactic nifedipine vs placebo administered 7 to 21 days after acute myocardial infarction, and showed that mortality and reinfarction rates in the group of patients randomly assigned to nifedipine did not differ from those assigned to placebo. Thrombolytic therapy was not provided to any patient in this cohort.

The second cohort comprises 1940 (1429 men, 74%) unselected patients from two prospective nationwide surveys, conducted in all 25 coronary care units (including the 13 centres from 1981–83) during January/February in 1992 (n=941 consecutive patients) and 1994 (n=999 consecutive patients), aimed to evaluate the management and outcome of acute myocardial infarction patients hospitalized in the coronary care units in Israel. Thrombolytic therapy and invasive coronary procedures were used at the discretion of the treating physician, and the main thrombolytic agent used was streptokinase (in 85% of the cases). The baseline characteristics, management and early- and late outcome of the patients in 1992 and 1994 were comparable. Demographic and medical data, including history, in-hospital course and complications, were recorded on prespecified forms for all patients in both cohorts, by dedicated study physicians in the coronary care units. Diagnosis of acute myocardial infarction was based on the presence of two of the following: typical chest pain lasting at least 30 min; new electrocardiographic changes (Q/QS and/or ST segment and T-wave changes), an increase in creatine kinase to more than twice the upper limit, or a concomitant rise in the creatine kinase MB isoenzyme level. The organization, data acquisition, data management and follow-up were performed in the same coordinating centre in both cohorts.

The medications reported in the 1981–83 cohort correspond to those given at discharge, whereas in the 1992–94 cohort, the medications reported correspond to those given at any time during the hospitalization stay.

Mortality rates at 30 days and at 1 year in both study periods were assessed from medical charts, phone calls and by matching the identification numbers of the patients with the Israeli National Population Register.

Statistical analysis

Statistical analysis was performed using SAS statistical software. Chi-square and t-tests were used to determine the significance of the differences between proportions and means, respectively, where appropriate. Results of continuous variables are reported as mean ± 1 SD. Two-sided *P* values are reported.

Direct age-adjustment was performed in order to compare mortality rates between the two periods (1992–94 vs 1981–83) in men and women. The standard population was the 1981–83 cohort (n=5839), where the age subgroups were: <55 years (22%), 55–64 years (31%), 65–74 years (34%) and ≥75 years of age (13%).

Survival curves were estimated using the method of Kaplan–Meier. The significance of the difference between the survival curves was assessed by the log-rank test (SAS LIFETEST Procedure). To control for age differences between patients in the 1992–94 cohort treated or not with thrombolysis and/or mechanical revascularization, age-adjusted survival curves were constructed using the SAS PHREG Procedure.

Table 1 Clinical characteristics of men and women in 1981–83 vs 1992–94

	Men			Women		
	1981–83 (n=4315)	1992–94 (n=1429)	*P**	1981–83 (n=1524)	1992–94 (n=511)	*P**
Patients in the cohort, %	74	74		26	26	
Age, year (mean ± SD)	61·4 ± 10·8	61·5 ± 12·4	0·78	67·3 ± 9·1	68·4 ± 10·3	0·04
Range	25–96	23–94		29–93	31–93	
≥70 (%)	1102 (26)	413 (29)	0·01	668 (44)	257 (50)	0·01
Patient history, n (%)						
Hypertension	1524 (36)	486 (34)	0·14	790 (53)	278 (54)	0·72
Diabetes	773 (18)	325 (23)	0·0001	435 (29)	181 (35)	0·003
Smoking	1634 (38)	631 (44)	0·0001	216 (14)	66 (13)	0·48
Prior MI	1114 (26)	447 (31)	0·0001	301 (20)	113 (22)	0·32
Prior angina	2074 (49)	398 (27)	<0·0001	794 (54)	157 (31)	<0·0001
Cerebrovascular accident	195 (5)	82 (6)	0·07	77 (5)	31 (6)	0·42
Killip ≥II on admission, n (%)	1337 (31)	389 (27)	0·007	607 (40)	191 (37)	0·32
Q-wave MI, n (%)	3655 (85)	1042 (73)	<0·0001	1214 (80)	368 (72)	0·0003
MI location, n (%)			0·74			0·19
Anterior	2006 (47)	655 (46)		732 (48)	232 (45)	
Inferior/posterior	1777 (41)	609 (43)		606 (40)	224 (44)	
Lateral	255 (6)	77 (5)		92 (6)	21 (4)	
Undetermined	277 (6)	88 (6)		98 (6)	34 (7)	

MI=myocardial infarction.
*Comparing 1981–83 and 1992–94 cohorts.
In the 1981–83 cohort missing values were recorded for some variables (history of hypertension, prior MI, prior angina, cerebrovascular accident, and Killip class on admission) in less than 3% of the cases. The percentages reported were calculated without missing values.

To compare 30-day mortality in the two periods, in both sexes separately, in terms of odds-ratio (OR) with 95% confidence interval (CI), multivariate stepwise logistic regression analyses (SAS LOGISTIC Procedure) were performed, adjusting for age, hypertension, diabetes mellitus, prior infarction, prior angina, anterior infarct location, Q-wave acute myocardial infarction, Killip class ≥II on admission and/or heart failure during the index hospitalization, history of stroke, 'period' (where the 1981–83 cohort was the reference group, OR=1) and 'centre' (where the 13 coronary care units that participated in both cohorts in 1981–83 and in 1992–94 were the reference group, OR=1). Stepwise Cox proportional-hazard regression models (SAS PHREG Procedure) adjusting for the same variables were used to compare the first-year mortality in 30-day survivors and cumulative first-year mortality in 1992–94 vs 1981–83, in terms of hazard ratio (HR; 95% CI). A variable was allowed to enter into the model if it made a significant contribution at the $P=0{\cdot}15$ level of significance, and was removed if after subsequent addition of other variables, it no longer made a contribution at the $P=0{\cdot}10$ level. Since the study was too small to assess the role of individual therapeutic modalities thought to be associated with improved survival, the variable 'period' was introduced in the multivariate models. An alternative analytic approach was undertaken with adjustments for the same variables and the variable 'reperfusion therapy' (thrombolysis and/or mechanical revascularization) to determine the adjusted mortality decline separately in 'reperfused' and 'non-reperfused' patients in 1992–94 vs patients in 1981–83.

Results

Baseline characteristics

The proportion of men and women hospitalized in the coronary care units in the two periods was similar (74% men). The clinical characteristics of the men and women of the two cohorts were comparable (Table 1). The mean age of women in 1992–94 was slightly higher than in 1981–83. In both sexes the proportion of elderly patients increased from 1981–83 to 1992–94. In men and women the prevalence of diabetes and non-Q wave acute myocardial infarction was higher in 1992–94 than in 1981–83, while the prevalence of prior angina and Killip class ≥II on admission declined. In 1992–94, the prevalence of smoking and prior myocardial infarction was higher in men, but not in women. In both sexes infarct location was similar in both periods.

In-hospital complications

In both sexes in-hospital complications were lower in 1992–94 than in 1981–83 (Table 2). The incidence of asystole, ventricular tachycardia or ventricular fibrillation, high-grade atrioventricular block, congestive heart failure and cardiogenic shock declined in both sexes in 1992–94. In addition, a decline in the incidence of paroxysmal atrial fibrillation and acute mitral

Table 2 In-hospital complications of men and women in 1981–83 vs 1992–94

	Men			Women		
	1981–83 (n=4315) n (%)	1992–94 (n=1429) n (%)	*P**	1981–83 (n=1524) n (%)	1992–94 (n=511) n (%)	*P**
Asystole	268 (6)	43 (3)	<0·0001	176 (12)	22 (4)	<0·0001
Ventricular tachycardia/fibrillation	1012 (23)	168 (12)	<0·0001	262 (17)	48 (9)	<0·0001
Paroxysmal atrial fibrillation	532 (12)	112 (8)	<0·0001	219 (14)	74 (14)	0·95
Second-, third-degree atrioventricular block	439 (10)	100 (7)	0·0004	196 (13)	52 (10)	0·11
Congestive heart failure	885 (21)	207 (14)	<0·0001	389 (26)	84 (16)	<0·0001
Cardiogenic shock	296 (7)	66 (5)	0·003	197 (13)	55 (11)	0·20
Recurrent ischaemia	388 (9)	166 (12)	0·004	127 (8)	51 (10)	0·25
Recurrent myocardial infarction	157 (4)	43 (3)	0·26	81 (5)	17 (3)	0·07
Acute mitral regurgitation	86 (2)	14 (1)	0·01	51 (3)	14 (3)	0·50
Cerebrovascular accident	39 (0·9)	10 (0·7)	0·47	15 (1)	6 (1·2)	0·71

*Comparing 1981–83 and 1992–94 cohorts.
$P<0·0001$ for both sexes, when comparing all complications in 1981–83 vs 1992–94 (by MANOVA).

Table 3 Management of men and women in 1981–83 vs 1992–94

	Men			Women		
	1981–83 (n=4315) n (%)	1992–94 (n=1429) n (%)	*P**	1981–83 (n=1524) n (%)	1992–94 (n=511) n (%)	*P**
Medications†						
Nitrates	1604 (43)	972 (68)	<0·0001	557 (50)	342 (67)	<0·0001
Beta-blockers	643 (17)	546 (38)	<0·0001	209 (19)	171 (33)	<0·0001
Aspirin	124 (3)	1141 (80)	<0·0001	23 (2)	367 (72)	<0·0001
Anticoagulants	67 (2)	1004 (70)	<0·0001	18 (2)	343 (67)	<0·0001
Calcium antagonists	1299 (35)	282 (20)	<0·0001	344 (31)	98 (19)	<0·0001
Digitalis	440 (12)	116 (8)	<0·001	186 (18)	59 (12)	0·008
ACE-inhibitors	—	410 (29)	—	—	133 (26)	—
Thrombolysis	—	647 (45)	—	—	200 (39)	—
Procedures						
Pacemaker	517 (12)	67 (5)	<0·0001	247 (16)	30 (6)	<0·0001
Swan–Ganz catheter	273 (6)	28 (2)	<0·0001	105 (7)	15 (3)	0·001
Coronary angiography	31 (1)	396 (28)	<0·0001	16 (1)	103 (20	<0·0001
PTCA	—	163 (11)	—	—	45 (9)	—
CABG	—	59 (4)	—	—	14 (3)	—

ACE=angiotensin converting-enzyme; CABG=coronary artery bypass graft surgery; PTCA=percutaneous transluminal coronary angioplasty.
*Comparing 1981–83 and 1992–94 cohorts.
†In 1981–83 the numbers reported are at discharge, including 3688 men and 1120 women (see Methods).

regurgitation was noted in men and of recurrent myocardial infarction in women. On the other hand, the incidence of recurrent ischaemia increased in both sexes in 1992–94.

Management

Compared to 1981–83, in 1992–94 men and women were treated more frequently with nitrates, beta-blockers, aspirin and anticoagulants, while they received calcium antagonists and digitalis less often (Table 3). ACE-inhibitors, not available in 1981–83, were similarly used in men and women in 1992–94. Thrombolytic therapy, which was not in use in 1981–83, was given to 45% of the men and 39% of the women in 1992–94 ($P=0·02$). Coronary angiography during the hospitalization period, performed in less than 1% of patients in 1981–83, increased to 28% (24% in 1992 and 31% in 1994) in the men, and to 20% (16% in 1992 and 23% in 1994) in the women in 1992–94. In 1981–83, PTCA and CABG were not performed during the index hospitalization, while in 1992–94, PTCA was performed in 11% (8% in 1992 and 15% in 1994) of the men and 9% (6% in 1992 and 11% in 1994) of the women, and CABG in 4% of the men and 3% of the women.

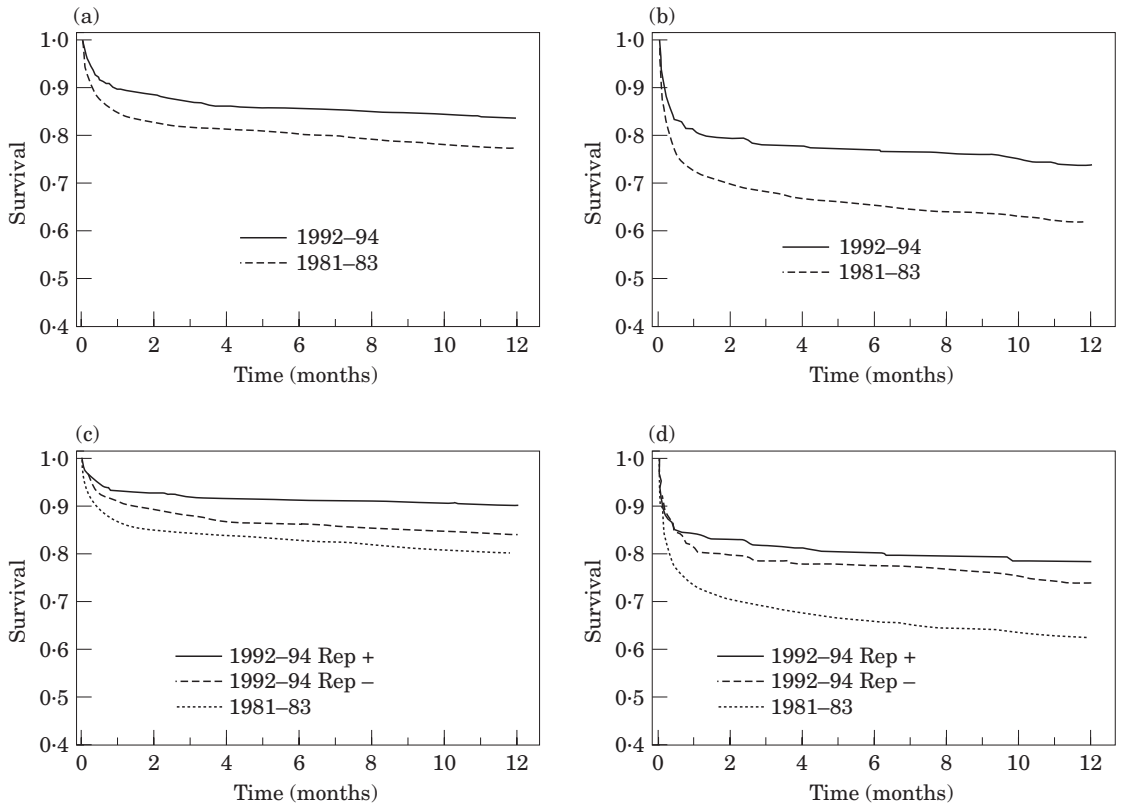

Figure 1 **Upper panel: Cumulative 1-year Kaplan–Meier survival curves of patients in the 1981–83 and 1992–94 cohorts, in men (a) and women (b). A significant decline in mortality was evident in both sexes in 1992–94; $P<0{\cdot}0001$ by the log-rank test. Lower panel: One-year age-adjusted survival curves of patients in the 1981–83 cohort vs 'reperfused' (Rep+) and 'non-reperfused' (Rep −) in the 1992–94 cohort, in men (c) and in women (d). ('reperfusion'=thrombolysis and/or mechanical revascularization).**

Mortality

Mortality rates were significantly lower in 1992–94 than in 1981–83 in both sexes. The 30-day, 30-day to 1-year, and the cumulative 1-year crude mortality rates declined, in men, from 15·7% to 10·5% ($P<0{\cdot}0001$), from 8·4% to 6·6% ($P=0{\cdot}05$), and from 22·8 to 16·4% ($P<0{\cdot}0001$), respectively. In women mortality also declined significantly, from 27·5% to 19·2% ($P=0{\cdot}0002$), from 14·4% to 9·0% ($P=0{\cdot}005$), and from 37·9% to 26·4% ($P<0{\cdot}0001$), respectively. The cumulative 1-year Kaplan–Meier survival curves are presented in Fig. 1(a) and (b). The direct age-adjusted mortality rates and the multivariate-adjusted odds ratios and hazard ratios are presented in Table 4. After multiple adjustment (see Methods) the 30-day, 30-day to 1-year and the cumulative 1-year mortality declined by 31% (OR=0·69), 26% (HR=0·74) and 30% (HR=0·70), respectively, in men, and by 30% (OR=0·30), 46% (HR=0·54) and 33% (HR=0·67), respectively, in women (Table 4). In both periods studied, the mortality rates were higher in women than in men (Table 4). In 1992–94, the covariate-adjusted 1-year cumulative mortality risk (Cox regression model) was 1·35 fold higher in women than in men (HR=1·35; 95% CI 1·22–1·51). Nevertheless, the cumulative 1-year mortality declined similarly by ≈30%, in both sexes.

Among the 1992–94 cohort, the decline in mortality compared to the 1981–83 cohort was more marked in patients treated by thrombolysis and/or mechanical revascularization ('reperfused patients') (Table 5 and Figs 1(c) and (d), 2(a) and (b)). To control for age differences between men ($59{\cdot}7 \pm 11{\cdot}9$ vs $63{\cdot}6 \pm 12{\cdot}6$ years, respectively, $P<0{\cdot}0001$) and women ($65{\cdot}5 \pm 10{\cdot}2$ vs $70{\cdot}9 \pm 9{\cdot}9$, respectively, $P<0{\cdot}0001$) treated or not with thrombolysis and/or mechanical revascularization, age-adjusted survival curves were constructed (Fig. 1(c) and (d)). The direct age-adjusted mortality rates and the multivariate-adjusted odds ratios and hazard ratios are presented in Fig. 2(a) and (b) and Table 5. After multivariate adjustment the 30-day, 30-day to 1-year and the cumulative 1-year mortality declined in men treated by thrombolysis and/or mechanical revascularization in the 1990s compared to the 1980s by 38% (OR=0·62), 59% (HR=0·41) and 44% (HR=0·56), respectively, and in women by 43% (OR=0·57), 48% (HR=0·52) and 39% (HR=0·61), respectively (Table 5).

Table 4 Direct age-adjusted mortality rates and multivariate-adjusted relative risk in 1992–94 vs 1981–83, in men and women

	Men			Women		
	Age-adjusted mortality % (95% CI)		Multivariate	Age-adjusted mortality % (95% CI)		Multivariate
Mortality	1981–83 (n=4315)	1992–94 (n=1429)	RR* (95% CI) 1992–94 vs 1981–83	1981–83 (n=1524)	1992–94 (n=511)	RR* (95% CI) 1992–94 vs 1981–83
30-day	17·0 (15·9–18·1)	10·8 (9·2–12·4)	0·69 (0·55–0·87)	24·0 (21·8–26·3)	15·1 (12·0–18·2)	0·70 (0·52–0·94)
30-day to 1-year	9·1 (8·2–10·1)	6·7 (5·3–8·1)	0·74 (0·58–0·96)	12·5 (10·4–14·5)	6·8 (4·5–9·2)	0·54 (0·38–0·79)
1-year cumulative	24·6 (23·3–25·9)	17·0 (15·0–18·9)	0·70 (0·60–0·81)	33·6 (31·1–36·1)	21·0 (17·5–24·4)	0·67 (0·55–0·81)

*Relative risk (RR) for mortality of patients in 1992–94 as compared to patients in 1981–83 (odds ratio for 30-day mortality, and hazard ratio for 1-year mortality in 30-day survivors and for cumulative 1-year mortality) after adjusting for: age, hypertension, diabetes, prior myocardial infarction, prior angina, anterior infarct location, Q wave myocardial infarction, Killip class on admission or heart failure during the index hospitalization, history of stroke, and 'centre' (by means of multivariate stepwise regression models; see Methods).

A milder decline in mortality was also evident among patients not treated by thrombolysis and/or mechanical revascularization ('non-reperfused'), in 1992–94, compared with patients in 1981–83. In men, the cumulative 1-year direct age-adjusted mortality rate declined from 24·6% to 21·1% (HR=0·87) as the result of the decline in 30-day mortality from 17·0% to 12·1% (OR=0·77; Table 5 and Figs 1(c) and 2(a)). In women, this decline in the cumulative 1-year direct age-adjusted mortality was of greater magnitude, from 33·6% to 23·9% (HR=0·71; Table 5 and Figs 1(d) and 2(b)).

Discussion

The present study demonstrates that in 1992–94, men and women hospitalized in coronary care units in Israel with acute myocardial infarction exhibited fewer in-hospital complications and lower early and 1-year mortality rates than in 1981–83. Despite higher mortality, in both periods in women than in men, the cumulative 1-year mortality declined similarly in both sexes by ≈30%. The decline in mortality was more marked in patients treated by thrombolysis and/or mechanical revascularization. The similar decline in mortality in both sexes suggests that the implementation in daily practice of new therapeutic modalities proven effective in clinical trials after acute myocardial infarction, has exerted a similar favourable impact on prognosis in men and in women.

Baseline characteristics

The baseline characteristics in both periods in men and women were comparable, however, some differences were noted. In both sexes the proportion of elderly patients, the prevalence of diabetes, prior myocardial infarction and non-Q wave acute myocardial infarction slightly increased from 1981–83 to 1992–94, whereas the prevalence of prior angina and Killip class ≥II on admission declined. These differences, which may be associated with worse prognosis, were taken into consideration in the multivariate analyses (Tables 3 and 4 and Fig. 1). The higher prevalence of non-Q wave acute myocardial infarction is in accordance with other studies[13,28,30,31], and may be related to the administration of thrombolytic therapy, aspirin, and beta-blockers, which may abort the progression to Q wave acute myocardial infarction[28,31], or to the improved methods for diagnosing acute myocardial infarction, including increased use of creatine kinase-MB enzyme[28,30]. The increased prevalence of non-Q wave acute myocardial infarction may also be related to changes in hospitalization policy in recent years, in which patients with non-Q wave acute myocardial infarction are admitted more often to the coronary care units, because of the recognition that this type of acute myocardial infarction is associated with early recurrent infarction and an unfavourable post-discharge outcome compared to patients with Q wave acute myocardial infarction[32]. The better Killip class on admission may be related to faster arrival in hospital, to better pre-hospital management by mobile coronary care unit, or to the better management prior to the index acute myocardial infarction. This latter reason may also explain the lower prevalence of prior angina in the 1990s.

Mortality

In previous reports from Israel[33,34] we documented a substantial improvement in both early- and 1-year survival among patients hospitalized with acute myocardial infarction from 1966 to 1981–83 to 1992, which was more marked in the elderly[35,36]. However, it was unclear whether the decline in mortality was parallel in

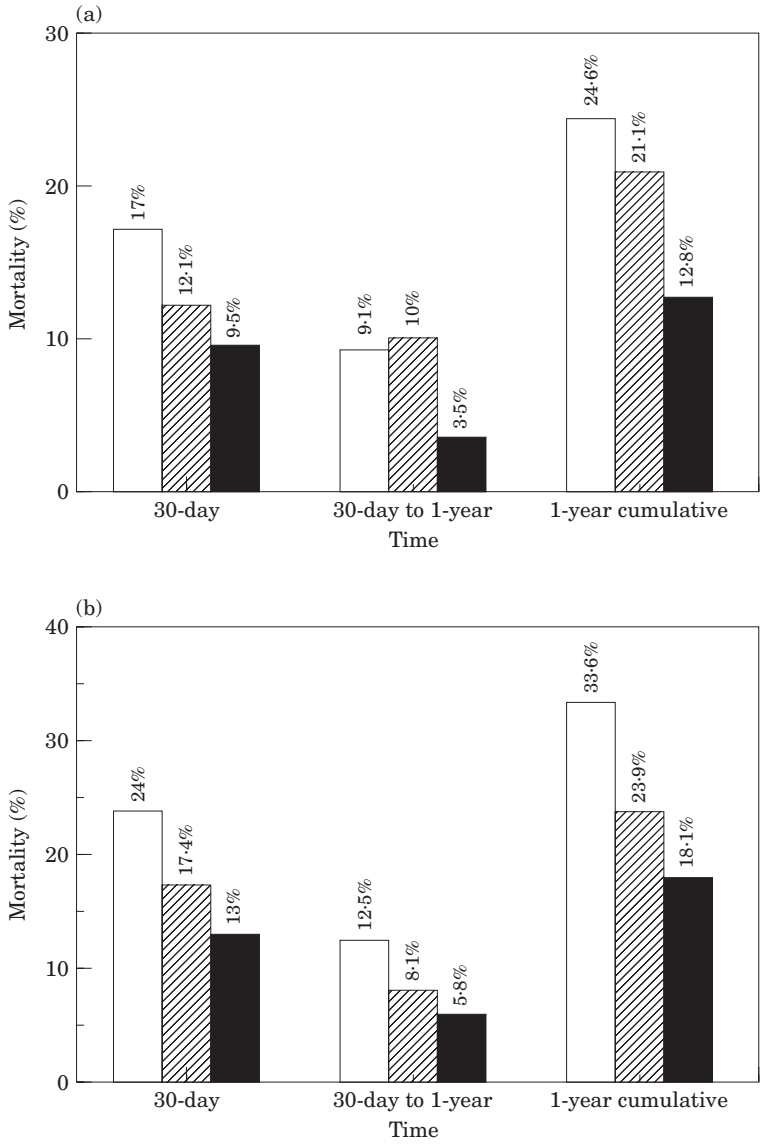

Figure 2 **Thirty-day, 30-day to 1-year, and cumulative 1-year direct age-adjusted mortality rates in 1981–83 (□) and for 'reperfused' (■) and 'non-reperfused' (▨ patients in 1992–94, in men (a) and in women (b)).**

men and women. In the current study we document a substantially improved survival of similar magnitude (≈30%) in both sexes during the last decade. Changes in medical management (i.e. increase in use of heparin, aspirin, beta-blockers, ACE-inhibitors, etc.), the use of thrombolytic therapy with adjuvant mechanical revascularization procedures, and other unmeasurable factors may have contributed to the better outcome of patients hospitalized with acute myocardial infarction in the 1990s. These alterations in medical practice also probably contributed to the lower rate of in-hospital complications in 1992–94.

Despite the similar mortality decline in both sexes by ≈30%, the mortality rates in both periods remained higher in women vs men even after multiple adjustments, similar to other reports[22,23,26,27]. The higher mortality rates in women may arise from age differences (women were older than men by 7 years), higher prevalence of unfavourable comorbidities (i.e. hypertension, diabetes), and perhaps unmeasurable parameters (i.e. disease severity, late presentation, etc.). These differences in mortality rates between sexes may persist even after adjustment for age and other confounders (HR=1·35 for 1-year cumulative mortality in men vs women in 1992–94). Nevertheless, the mortality rates of men and women hospitalized with acute myocardial infarction in the coronary care units in the 1990s in Israel were lower than a decade ago.

In the present study, the main improvement in survival between the two periods was achieved early after the acute myocardial infarction and was followed by further improvement during the first post-infarction

Table 5 Direct age-adjusted mortality rates and multivariate-adjusted relative risk of 'non-reperfused' and 'reperfused' men and women in 1992–94 vs 1981–83

	Men					Women				
	Age-adjusted mortality (%)			Multivariate RR* (95% CI)		Age-adjusted mortality (%)			Multivariate RR* (95% CI)	
		1992–94					1992–94			
Mortality	1981–83 (n=4315)	Non-reperfused (n=672)	Reperfused (n=757)	1992–94 Non-reperfused vs 1981–83	1992–94 Reperfused vs 1981–83	1981–83 (n=511)	Non-reperfused (n=276)	Reperfused (n=235)	1992–94 Non-reperfused vs 1981–83	1992–94 Reperfused vs 1981–83
30-day	17·0	12·1	9·5	0·77 (0·57–1·02)	0·62 (0·45–0·84)	24·0	17·4	13·0	0·81 (0·56–1·17)	0·57 (0·37–0·88)
30-day to 1-year	9·1	10·0	3·5	1·08 (0·80–1·44)	0·41 (0·26–0·68)	12·5	8·1	5·8	0·56 (0·36–0·89)	0·52 (0·30–0·90)
1-year cumulative	24·6	21·1	12·8	0·87 (0·72–1·06)	0·56 (0·44–0·70)	33·6	23·9	18·1	0·71 (0·56–0·90)	0·61 (0·45–0·82)

*Relative risk (RR) for mortality of non-reperfused and reperfused patients in 1992–94 as compared to patients in 1981–83 (odds ratio for 30-day mortality, and hazard ratio for 1-year mortality in 30-day survivors and for cumulative 1-year mortality) after adjusting for: age, hypertension, diabetes, prior myocardial infarction, prior angina, anterior infarct location, Q wave myocardial infarction, Killip class on admission or heart failure during the index hospitalization, history of stroke, 'centre' and thrombolysis and/or mechanical revascularization (by means of multivariate stepwise regression models; see Methods).
'Reperfusion'=thrombolysis and/or mechanical revascularization.

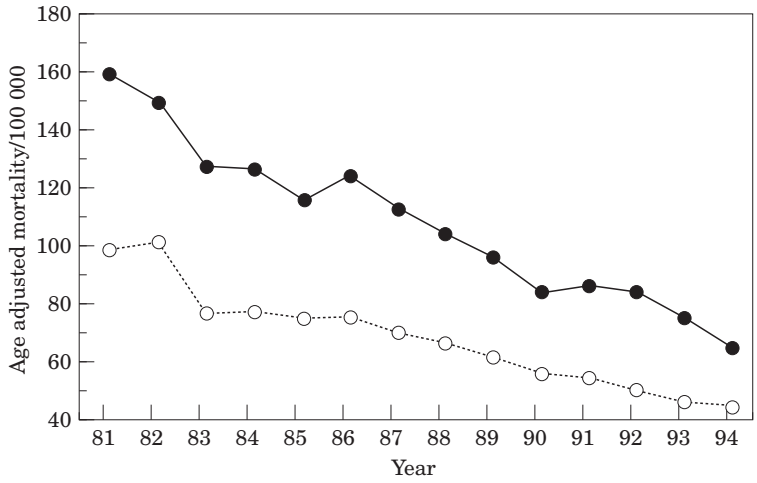

Figure 3 **Age-adjusted mortality rates from acute myocardial infarction (ICD-9-CM, code 410) in men (——) and women (– – –) residents of Israel, between 1981 and 1994. In both sexes mortality declined by ≈50%.**

year, an improvement that was more marked in patients treated with thrombolysis and/or mechanical revascularization ('reperfusion') (Table 5 and Figs 1(c) and (d), 2(a) and (b)). This finding suggests an extra benefit in these patients after 30 days, although in large-scale studies post-discharge survival of thrombolysed and control patients was similar[37]. Such improvement could be attributed to differences in the use of diagnostic and therapeutic procedures in the hospital or after discharge, or to the greater emphasis on secondary prevention measures (such as smoking cessation, lipid lowering medications, dietary changes, and aspirin use).

Although exclusion from thrombolytic therapy and mechanical revascularization procedures may have placed these patients in 1992–94 at increased risk, their improved prognosis compared with those patients hospitalized in 1981–83 (Table 5), suggests a beneficial effect of new therapeutic modalities introduced since the early 1980s or their modified use, such as increases in the use of aspirin, heparin, beta-blockers, and ACE-inhibitors, and a decrease in the use of calcium antagonists and digitalis. In the current study, in-hospital use of aspirin, heparin, and beta-blockers among patients not treated with thrombolysis and/or mechanical revascularization in 1992–94 was relatively low (68%, 42%, and 26%, in men; and 58%, 43%, and 23%, in women, respectively; data not tabulated), yet higher than in the early 1980s. Similar trends were reported in other studies[7,8,10,38,39]. Furthermore, ACE-inhibitors were not in use in 1981–83, but by 1992–94 they were given to ≈30% of men and women.

Interestingly, compared to the early 1980s, the decline in mortality among patients not treated with thrombolysis and/or mechanical revascularization in 1992–94 was more marked in women than in men (Table 5). This finding may be partly explained by the fact that women were older than men by 7 years, exhibiting a worse baseline profile (Table 1). As the beneficial effect of these medications after acute myocardial infarction is more marked in high risk patients with other comorbidities and in the elderly[4,5,40,41–43], the greater benefit observed in women is quite reasonable.

Of interest is the fact that mortality after acute myocardial infarction among coronary care unit patients in Israel declined even though the proportion of admitted elderly patients increased in the 1992–94 cohort. This was highlighted in our recent report, showing a significant improvement in the prognosis of elderly acute myocardial infarction patients during the last decade, in both those treated or not with thrombolysis and/or mechanical revascularization, but more marked in the former[35,36]. This finding is in accordance with data published by Naylor and Chen[8] and Dellborg *et al.*[7] showing greater reduction in mortality in elderly patients, and in discordance with others[16,20] who noted a greater reduction in mortality in young patients.

Previous studies

In the present study, 30-day mortality declined by ≈30% in about 10 years, in both sexes (Table 4). Similar trends in declining mortality early after acute myocardial infarction were reported in other countries in Europe[7,11,14,16,18,22] and North America[8–10,13,15,17,21], and were also attributed to changes in patient management, the expanded use of effective therapies, including thrombolytic agents, PTCA, anticoagulants, aspirin, beta-blockers and ACE-inhibitors[7,8,10,11,13,15–18,21,22].

However, only a few of these studies evaluated these trends separately in men and women[8,9,15–17,21,22]. Naylor and Chen[8] reported a 27% overall relative reduction in in-hospital case-fatality rate from acute myocardial infarction after adjustment for age and gender, in Ontario, Canada, between 1981 and 1991, that was more marked in women and in elderly patients.

Greenbaum *et al.*[16] reported a 46% overall relative decline in in-hospital mortality from acute myocardial infarction after adjustment for age and gender, in the North West Thames health region, in England, between 1979 and 1991. The decline in mortality was similar in men and women and more marked in young patients. The National Hospital Discharge Survey in the US[9] found a decline of about one third in the in-hospital case-fatality rate for acute myocardial infarction between 1985 and 1990. The decline in mortality was slightly lower in women than in men. In contrast, in a recent publication from four communities in the US, Rosamond *et al.*[21] reported that the annual decline in age-adjusted 28-day case-fatality rate for acute myocardial infarction between 1987 and 1994, was higher in women (9·8%) than in men (4·1%).

Data comparing the early- and post-discharge outcome of patients with acute myocardial infarction before and after the advent of the reperfusion era are scarce[15,17,22]. In a recent publication from Göteborg, Sweden, Abrahamsson *et al.*[22] reported a decline in the 2-year mortality after acute myocardial infarction from 36% in 1984 to 24% in 1991, which was more marked in women than in men. Le Feuvre *et al.*[15] noted that in-hospital mortality after acute myocardial infarction in Hamilton, Ontario, Canada, declined from 16% in 1986–87 to 9% in 1991–92. The decline in mortality was slightly more marked in women than in men. One-year mortality in hospital survivors did not change during this period and remained 12%, discordant to our study. McGovern *et al.*[17] reported a substantial decline in mortality in acute myocardial infarction patients hospitalized between 1985 and 1990 in the Minnesota Heart Survey. After adjustment for age and previous myocardial infarction, 28-day mortality, 3-year mortality among patients surviving to day 28, and cumulative 3-year mortality, declined by ≈25%, in men, and by 16% in women.

Study limitations

This study has several limitations. This is an observational study, and therefore, we cannot establish with certainty a causal relationship between different medical variables and treatments and patient outcomes. The decision of how to treat was not randomized, and was left to the discretion of the treating physician. Some differences in baseline characteristics associated with worst prognosis were noted between the two periods studied (see above). Finally we cannot exclude the possibility that better emergency response with faster arrival to hospital resulted in less severe presentation (i.e. a better Killip class on admission) or of less sick patients in the 1990s. In addition, the increased availability of coronary care unit beds, in the 1990s, may have resulted in the selection of less severely ill patients, or to the hospitalization of more patients with a non-Q wave myocardial infarction. Although these differences were taken into consideration in the multivariate analyses, some imbalances between the groups compared could not fully be controlled for and may remain.

The current study included 13 coronary care units operating in Israel in 1981–83 and all 25 units operating in 1992–94. To eliminate the potential bias of centre, a comparison of the same 13 units operating in both periods with the other 12 units was performed. Overall, there was a remarkable similarity between these two groups in baseline characteristics, management and early- and 1-year outcome, as published previously[34]. Also, in the multivariate analyses 'centre' was entered as one of the variables adjusted for in the models (see Methods), and turned out to be not statistically significant. This lends credence to the appropriateness of a comparison of the original 13 centres in 1981–83 and the 25 centres in 1992–94.

The present study was not a population-based survey, but rather compared the early and 1-year case-fatality rates of acute myocardial infarction patients hospitalized in the coronary care units in Israel in 1981–83 and 1992–94. Patients hospitalized in non-coronary care unit beds and patients who died out-of-hospital were not included. Despite the similar decline in case-fatality rates of men and women hospitalized with acute myocardial infarction in the coronary care unit, we cannot exclude the possibility that out-of-hospital death trends were different in men and women, as was suggested by the WHO MONICA Project[44] and the Minnesota Heart Survey[17]. Since out-of-hospital deaths were not recorded in either 1981–83 or in the 1992–94 cohorts, we looked at trends in age-standardized mortality rates from acute myocardial infarction, using ICD-9-CM code 410[45] among all residents of Israel during the years 1981–1994[46]. During that period, mortality from acute myocardial infarction declined similarly in both sexes, by ≈50% (Fig. 3), indirectly supporting the view that the decline, in both in-hospital and out-of-hospital mortality from acute myocardial infarction, was of similar magnitude in men and women.

Finally, we cannot exclude the possibility that it is not the management of patients in the coronary care unit which is responsible for the decline in mortality between the two cohorts, but rather perhaps undefined population factors. However, this issue was beyond the scope of our study.

In spite of these limitations, the findings of this study are interesting because we compared two cohorts of unselected acute myocardial infarction patients hospitalized in the majority of the coronary care units operating in 1981–83 and from all units operating in 1992–94 in Israel, representing the changes in hospital course, treatment strategies, and patient outcome in men and women after acute myocardial infarction over a decade.

Conclusion

During the last decade, the prognosis of acute myocardial infarction patients hospitalized in the coronary care

units in Israel improved considerably, with a similar decline in 1-year mortality by ≈30%, despite higher mortality in both periods in women compared to men. The main improvement in survival was achieved early after the acute myocardial infarction, with further improvement during the first post-infarction year. The decline in mortality was more marked in patients treated by thrombolysis and/or mechanical revascularization. The implementation in daily practice of new therapeutic modalities proven to be effective in clinical trials after acute myocardial infarction, probably played a major role in this favourable outcome in both sexes. Sex-specific assessment of patient outcome over time provides complementary prognostic evaluation after acute myocardial infarction.

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